Remarks

Claims 62, 64-65, 67, 69-74 and 80-89 presently appear in this case. No claims have been allowed. The Official Action of December 16, 2010, has now been carefully studied. Reconsideration and allowance are hereby respectfully urged.

Briefly, the present invention relates to a method for the treatment of a disease or disorder of the mucosa by administering a medicament to the GI tract of a subject having a disease or disorder associated with inflammation of the GI mucosa. The medicament is administered in an amount effective to achieve topical treatment of the GI mucosa. The medicament consists of lipid assemblies loaded with an active ingredient. The active ingredient is not covalently bound with the lipid assemblies. The lipid assemblies consist of a collection of lipids including one or more anionic lipid in an amount such that the net charge of the lipid assembly is negative. The lipid assemblies are optionally combined with one or more lipid assembly stabilizers. The invention is also directed to a method of directing delivery of an active ingredient effective for the topical treatment of an inflamed area of the gastrointestinal (GI) tract of a patient having a disease or disorder of the mucosa associated with inflammation of the GI mucosa.

Claims 62-64, 62,64-65,67,69-75 and 80 have been rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treatment of inflammation, does not reasonably provide enablement for treatment or prevention of diseases or disorders of mucosa. The examiner states that the independent claim does not recite any particular drug. The examiner states that all tumors cannot be treated with the same therapy. The examiner states that the claims are very broad in terms of the diseases to be treated. This rejection is respectfully traversed.

The present invention is directed to a novel carrier for known active ingredients. No novel active ingredients are disclosed herein. The present invention is applicable to any active ingredient that can be used to topically treat a condition associated with inflammation of the GI tract. The present invention is based on the discovery that active-ingredient loaded lipid assemblies can be targeted directly to the inflamed portion of the GI tract by use of negatively charged lipid assemblies. To clarify this intent, new claim 89 has been presented that is directed to a method of directing delivery of an active ingredient to an inflamed area of the GI tract. It does not matter what the active ingredient is, as long as it is one that is effective for the topical treatment of an inflamed area of the GI mucosa and the

patient is one having a disease or disorder associated with inflammation of the GI mucosa. The specification includes many examples of such known active ingredients.

To facilitate withdrawal of this rejection and early allowance of this case, claim 75, listing various diseases associated with inflammation of the GI mucosa, has now been deleted. The many examples of conditions that may be treated and active ingredients known to be able to treat such conditions as appear in the specification, for example, at page 14, line 20, through page 15, line 29, are sufficient to support the claimed genus. It is not necessary to include a dependent claim specifically listing such conditions. They are still covered by the independent claims.

It should be noted that the claims do not suggest that every cancer can be treated with one drug. Various drugs are disclosed for various conditions. Any drug known to be topically effective to treat a disease associated with inflammation of the GI mucosa can be delivered by means of the present invention in order to treat that condition.

For all of these reasons, those of ordinary skill in the art would be able to deliver any known active ingredient to the site of inflammation in the GI mucosa by means of the present invention without undue experimentation.

Reconsideration and withdrawal of this rejection are therefore respectfully urged.

Claims 62, 64-65, 67, 69-75 and 80 have been rejected under 35 U.S.C. 112, second paragraph, as being indefinite. The examiner states that the terminology used to describe the manner of administration is confusing since it is unclear as to how the composition is administered in view of the fact that the gastrointestinal system includes stomach, duodenum, small intestines and colon. The examiner questions how one can one administer the composition topically to the GI mucosa and what the term "in a manner" denotes. The examiner also states that the dependent claim 69 recites nausea and reflux and it is unclear how these are mucosal diseases or conditions. The examiner further states that "derivatives of 5-aminosalicylic acid" is unclear. This rejection is respectfully traversed.

As to the manner of administration, the specification explains the preferred manners of administration to achieve delivery to the GI tract. See page 20, lines 7-14, for example. Those of ordinary skill in the art, particularly in light of the above disclosure in the specification, are well aware of how to get drugs to the GI tract. It is preferably done orally or rectally. To clarify the claim language, the claims have been amended to specify that the

medicament is administered to the GI "tract," as opposed to the "mucosa." Delivery to the GI tract will inherently cause administration to the GI mucosa (which lines the tract). As it is common to deliver medicaments to the GI tract, it is hoped that this new language will help to obviate this rejection. It is not confusing to deliver to the GI tract. The term "in a manner" has now been deleted, thus obviating this part of the rejection.

Furthermore, nausea and reflux have been deleted from claim 69 and the term "derivatives" no longer appears in the claims. Accordingly, reconsideration and withdrawal of this rejection are respectfully urged.

Claims 62, 64-65, 67, 69-75 and 80 have been rejected under 35 U.S.C. 102(a) as being anticipated by Qi. The examiner states that Qi teaches anionic liposomal compositions for the delivery of active agents within and/or beneath the mucosal membranes. This rejection is respectfully traversed.

The present claims have now been amended to define the medicament in such a way as to exclude the presence of any fusogenic protein or polypeptide, such as saposin. Accordingly, the presently worded claims are not anticipated by Qi. The medicament is now defined as "consisting of" lipid assemblies and an optional pharmaceutically acceptable

carrier. The lipid assemblies are defined as "consisting of" a collection of lipids, including anionic lipids and optional lipid assembly stabilizers. The lipid assemblies are loaded with active ingredients effective for the topical treatment of the GI mucosa. Saposin (or any other fusogenic protein or polypeptide) is not a lipid, nor is it a lipid assembly stabilizer, nor is it an active ingredient effective for the topical treatment of the GI mucosa. It is certainly not a pharmaceutically acceptable carrier. Accordingly, as the present claims now exclude the possible presence of saposin as part of the medicament, whether embedded in the surface of the liposome or otherwise, none of the present claims can be anticipated by Qi. Reconsideration and withdrawal of this rejection are therefore respectfully urged.

Claims 62, 64-65, 67, 69-75 and 80 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Qi. The examiner states that Qi does not teach the treatment of all the diseases claimed through examples. However, the examiner concludes that, in view of the suggestion of various active agents which could be incorporated and the guidance provided by Qi, it would have been obvious to one of ordinary skill in the art to prepare various compositions for the treatment of various diseases with a reasonable expectation of success. This rejection is respectfully traversed.

As discussed above with respect to the anticipation rejection, the present claims have now been worded in such a manner as to exclude any fusogenic protein or polypeptide, which is a critical component of the medicament of Qi. There is no motivation given in Qi to omit the most critical component of Qi's medicament. Accordingly, it would not be obvious to omit it. The examiner has not suggested otherwise. Accordingly, reconsideration and withdrawal of this rejection is respectfully urged.

Claim 67 has been rejected under 35 U.S.C. 103(a) as being unpatentable over Qi in combination with Iga or Fossheim or Dyvik or Schneider, individually or in combination. The examiner states that Qi teaches the use of phosphatidylserine to form the anionic liposomes, but Qi does not teach the use of phosphatidylglycerol or a saturated form of phosphatidylglycerol. The examiner considers that the use of DSPG instead of phosphatidylserine taught by Qi would have been obvious to one of ordinary skill in the art since Iga, Fossheim, Dyvik and Schneider teach that for the preparation of liposomes either phosphatidylserine or phosphatidylglycerol could be used. This rejection is respectfully traversed.

As discussed above, the present claims exclude the presence of saposin. No combination of Qi, Iga, Fossheim, Dyvik and Schneider would provide motivation to omit saposin

from the formulations of Qi, particularly as it is considered by Qi to be critical to its invention. Accordingly, for the same reasons as discussed with respect to the other prior art rejections, reconsideration and withdrawal of this rejection are respectfully urged.

Claims 62, 64-65, 67, 70, 72 and 75 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Kim or Baczynska. The examiner states that Kim teaches the *in vitro* cytotoxic effect of negatively charged liposomes containing (DSPG) on murine colon carcinoma cells (abstract, page 169, col. 1, *in vitro* growth inhibition of C-26 cells). Baczynska teaches surface charge and the association of liposomes with colon carcinoma cells. The examiner states that, according to Baczynska, when phosphatidylserine was incorporated into the lipid bilayer, the amount of liposomes associated with cells tended to increase along with the amount of negatively charged lipid present in the liposomal bilayer (abstract, page 874, negatively charged liposomes and discussion). The examiner concedes that these references do not teach the administration of the liposomes or the mode of administration. However, the examiner concludes that, since these references show the interaction of the liposomes to the colon carcinoma cells, it would have been obvious to one of ordinary skill in the art to choose an appropriate method of

administration so that they reach the colon, interact with these cells and deliver the anticancer drugs. This rejection is respectfully traversed.

The present claims require that the lipid assemblies be loaded with an active ingredient effective for the topical treatment of said GI mucosa. The Kim and Baczynska references do not disclose any such active ingredient being loaded in their liposomes. The examiner has not explained why it would be obvious to add such an active ingredient. Furthermore, the examiner has not explained why it would be obvious to use the liposomes of Kim or Baczynska as a means to deliver an active ingredient to an area of inflammation in the GI mucosa. Accordingly, reconsideration and withdrawal of this rejection are respectfully urged.

It is submitted that all of the claims now present in the case clearly define over the references of record and fully comply with 35 USC 112. Reconsideration and allowance are therefore earnestly solicited.

Respectfully submitted,

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